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SHORT REPORT

RISK OF MELANOMA AMONG RADIOLOGIC TECHNOLOGISTS IN THE UNITED STATES

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Our study examines the risk of melanoma among medical radiation workers in the U.S. Radiologic Technologists (USRT) study. We evaluated 68,588 white radiologic technologists (78.8% female), certified during 1926–1982, who responded to a baseline questionnaire (1983–1989) and were free of cancer other than nonmelanoma skin at that time. Participants were followed through completion of a second questionnaire (1994–1998). We identified 207 cases, 193 subjects who reported first primary melanoma and 14 decedents with melanoma listed as an underlying or contributory cause of death. We examined risks of occupational radiation exposures using work history information on practices, procedures, and protective measures reported on the baseline questionnaire. Based on Cox proportional hazards regression, melanoma was significantly associated with established risk factors, including constitutional characteristics (skin tone, eye and hair color), personal history of nonmelanoma skin cancer, family history of melanoma and indicators of residential sunlight exposure. Melanoma risk was increased among those who first worked before 1950 (RR = 1.8, 95% CI = 0.6–5.5), particularly among those who worked 5 or more years before 1950 (RR = 2.4; 0.7–8.7; *p* (trend) for years worked before 1950 = 0.03), when radiation exposures were likely highest. Risk was also modestly elevated among technologists who did not customarily use a lead apron or shield when they first began working (RR = 1.4; 0.8–2.5). Clarifying the possible role of exposure to chronic ionizing radiation in melanoma is likely to require nested case-control studies within occupational cohorts, such as this one, which will assess individual radiation doses, and detailed information about sun exposure, sunburn history and skin susceptibility characteristics.
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The incidence of cutaneous malignant melanoma has been increasing rapidly in the white population of the United States (U.S.)[1] with a lifetime risk of melanoma of about 2.0% in white men and 1.4% in white women.[2] The major established environmental risk factor for melanoma is solar radiation.[3–5] Host susceptibility factors include fair skin; blue eyes; blond or red hair; high numbers of nevi; a family history of melanoma; a personal history of skin cancer; and immunosuppression.[3,6,7]

Although acute and fractionated ionizing radiation have been linked to nonmelanoma skin cancer,[8] there is limited and inconsistent epidemiologic evidence concerning the relationship between ionizing radiation and cutaneous malignant melanoma, particularly at low-to-moderate, chronic doses.[8,9] In our study, we examined prospectively (1983–1998) the risk of cutaneous malignant melanoma from low-to-moderate, chronic exposure to ionizing radiation based on work history and other factors in the large U.S. Radiologic Technologists (USRT) cohort.

MATERIAL AND METHODS

The USRT study, an ongoing collaboration of the U.S. National Cancer Institute, University of Minnesota and the American Registry of Radiologic Technologists (ARRT) has followed up a nationwide cohort of 146,022 radiologic technologists residing in the United States and certified by ARRT for at least two years between 1926 and 1982.[10,11] Detailed information on the methods has been provided elsewhere.[10]

Briefly, during 1983–1989, all subjects located alive (n = 132,454) were mailed a baseline questionnaire, which collected information on work history and practices, demographic and lifestyle factors, reproductive and medical history, as well as other personal information. A second questionnaire, administered during 1994–1998, ascertained incident cancers, updated information on the risk factors previously evaluated and asked about skin tone, hair and eye color, as well as family medical history. The response rate to the first questionnaire was 68% (90,305), and 83% (70,859) of living respondents to the first questionnaire answered the second questionnaire.

Study population

The evaluation of melanoma risk was limited to white subjects who responded to the first questionnaire, were cancer-free (except for nonmelanoma skin cancer) at completion of the baseline questionnaire and who responded to the second questionnaire or died during the intervening period through August 1998 (n = 68,588). There were 3,306 non-white subjects who were excluded, among whom only 2 reported a diagnosis of melanoma.

Eligible cases were those who reported a diagnosis of cutaneous melanoma with onset between completion of the 2 questionnaires or subjects who completed a baseline questionnaire and died without completing the second questionnaire through August 1998, with melanoma reported as a cause of death on the death certificate. Only cases with first primary melanomas were eligible, unless the prior cancer was nonmelanoma skin cancer (n = 14 cases among the latter).

Pathology and other medical record information were requested to validate the self-reported melanomas. Among the 243 subjects reporting melanoma, medical records were obtained on 160 (66%). Of these 160, medical records validated the melanoma diagnosis for 140 subjects (88%). We excluded the 20 incorrectly reported

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"melanomas." The 140 validated melanomas, however, included diagnoses of 31 melanomas *in situ* and 4 ocular melanomas, which we excluded from the case definition. There was no significant difference by age, geographic region of residence or number of years worked as a radiologic technologist between those potentially eligible cases for whom medical records were and were not obtained. Because a high proportion of self-reported melanomas with medical records were validated, and receipt of medical records did not differ significantly by demographic or other factors, we included potentially eligible incident cases for whom no medical record confirmation could be obtained.

Decedents were included as cases because of the high (89%) confirmation rate for melanoma designated as cause of death on U.S. death certificates.[12] Because only first primary cases were eligible, decedents with melanoma and another cancer cause of death listed on the death certificate were included only if the average survival rate of melanoma exceeded that of the other cancer[13] and thus likely preceded it (1 case excluded). We included a total of 207 cases of melanoma, composed of 193 incident first primary melanomas and 14 deaths.

Job history and work practices

We evaluated melanoma risk according to respondents' answers to questions in the baseline questionnaire regarding lifetime job history because individual radiation dose estimates were not available. We assessed year first worked as a radiologic technologist because medical radiation workers employed in the earlier calendar time periods (prior to 1950) were reported to have substantially higher exposures[14,15] than those employed in more recent time periods (since 1980),[16] likely due, at least in part, to changes in the recommended exposure limits from 30 rem/year in 1934 to 15 rem/year in 1949 (bone marrow dose), which was lowered to 5 rem/year in 1958.[17] Because cumulative years worked, independent of the particular decades worked, may not be a good surrogate for cumulative exposure, we evaluated the number of years worked in different time intervals. We also evaluated year first worked with diagnostic, therapeutic or nuclear medicine radiologic procedures and other work practices and protective measures used.

Other risk factor information

Age, sex, personal diagnostic and therapeutic radiation exposures and potential residential ultraviolet radiation exposures were assessed using responses to the baseline questionnaire. Information about hair color, eye color, skin tone and family history of melanoma were only asked on the second questionnaire; therefore, this information was not available for subjects who died prior to the second questionnaire. A proxy measure for the potential mean annual adult residential exposure to sunlight was derived by using the estimated annual solar ultraviolet radiation assigned to each state[18] in which the radiologic technologist reported working weighted by the duration of working in that location. A proxy measure for the potential residential sunlight exposure in childhood was estimated as the annual solar ultraviolet radiation assigned to the state of birth. No information was available about residence during the subject's childhood, nor about the number of sunburns, skin reactions to sun exposure or number of nevi among subjects.

Statistical analyses

Participants were followed from the return date of the first questionnaire until death, the return date of the second USRT study questionnaire or the date of diagnosis of the first cancer (other than nonmelanoma skin), whichever occurred first. We used Cox proportional hazards regression to compute relative risks (RRs) with 95% confidence intervals (CIs), using age at diagnosis or death from melanoma as the response (*i.e.,* age as the time-scale beginning at completion of the first questionnaire)[19] and stratifying at baseline for birth cohort in 5-year intervals to control for secular trends. Subjects were censored at the date of the first cancer other than melanoma or nonmelanoma skin cancer, the date of the second questionnaire if no cancer was reported or the date of death from a cause other than melanoma. When assessing risk by age at baseline, we used calendar time as the time scale.

Subjects who died due to causes other than melanoma were considered to be non-cases. Deaths were included in the analysis despite the absence of some covariate information (*i.e.,* skin tone and hair color) for nonrespondents to the second questionnaire because these covariates did not substantially affect the findings when risks were estimated based on incident cases alone. Moreover, key findings on radiation risk were very similar when estimated based on incident cases excluding all deaths or based on incident cases and melanoma and other deaths. In addition, although diagnosis date was unavailable for decedents, mean follow-up time was similar for decedents (6.2 years) and incident cases (5.7 years). Missing information was coded as a separate category. Nonrespondents to the second questionnaire, for whom information about incident melanomas was unknown, were presumed alive (because tracing using the National Death Index, Social Security and other records found no evidence of death) and excluded from the analysis (14,874 subjects).

Multivariate models included established risk factors for cutaneous melanoma, *i.e.,* skin tone, hair color,[7] sex, since incidence rates differ by sex,[7] personal history of nonmelanoma skin cancer[20] and proxy measures for residential childhood and adult sunlight exposure, since both periods of exposure have been linked to melanoma in several epidemiologic studies.[21] When estimating risk associated with the decade subjects first worked as a radiologic technologist, we adjusted for the total number of years worked. In estimating risks for duration of employment during specific decade periods, we adjusted for duration of work during other decade periods. To assess risk by first use of procedures, we grouped together diagnostic procedures (fluoroscopy, dental x-ray, routine x-ray, multifilm procedures, CAT scan), therapeutic procedures (orthovoltage, cobalt 60, betatron, other x-ray teletherapy) and nuclear medicine procedures (diagnostic radioisotopes, radium therapy, other radioisotope therapy) and adjusted for first decade of performance of each of the other groups of procedures and number of years worked with the procedure that was performed longest in each group.

In an exploratory analysis, we examined interaction between sunlight exposure and years worked in the early years by stratifying the population between those with potentially lower and higher residential sunlight exposures. Because of the small number of subjects with early work exposures in each stratum defined by sunlight exposure, more detailed analysis was not pursued.

In calculating tests for trend, we modeled exposure variables as continuous, unless otherwise specified, and controlled for covariates. All *p*-values are 2-sided.

RESULTS

In our study population of white and cancer-free members of the USRT cohort, subjects were 79% female and 39% had completed 1 or more years of college at baseline (Table I). Most were relatively young, 45% under age 35 years, and only 3% were 65 years or older. Correspondingly, most had been certified as radiologic technologists during the 1970s and early 1980s (56%) and only 3% were certified before 1950. At the time of the baseline questionnaire, subjects resided in all the major regions of the United States (Table I). Follow-up covered 698,028 person-years.

Risk associated with constitutional and other factors not including ionizing radiation

Melanoma risk increased with age, but did not vary by gender (Table II). Constitutional factors (skin, eye and hair color), personal history of nonmelanoma skin cancer, family history of melanoma and the proxy measure for adult residential sunlight exposure were all significantly associated with melanoma. The slightly elevated risk seen for the highest level of the childhood sunlight

TABLE I – FREQUENCY OF SELECTED DEMOGRAPHIC AND OTHER CHARACTERISTICS AMONG WHITE MELANOMA CASES COMPARED WITH THE STUDY POPULATION OF WHITE RADIOLOGIC TECHNOLOGISTS IN THE U.S. RADIOLOGIC TECHNOLOGISTS STUDY COHORT[1]

Characteristics[2]	Melanoma cases		Study population	
	n = 207	%	n = 68,588	%
Age at baseline questionnaire				
>35 years	81	39.1	30,597	44.6
35–44 years	78	37.7	22,877	33.4
45–54 years	32	15.5	9,352	13.6
55–64 years	11	5.3	3,763	5.5
65+ years	5	2.4	1,999	2.9
Gender				
Female	159	76.8	54,045	78.8
Male	48	23.2	14,543	21.2
Education[3]				
High School (9–12 years)	4	1.9	519	0.8
Radiation technology program (2 years)	107	51.7	37,414	54.6
1+ years college/graduate school	88	42.5	26,696	38.9
Other	7	3.4	3,520	5.1
Year certified as radiation technologist				
<1950	9	4.4	1,951	2.8
1950-59	29	14.0	8,299	12.1
1960-69	58	28.0	20,052	29.2
1970-79	101	48.8	34,669	50.6
1980+	10	4.8	3,617	5.3
Residence at baseline questionnaire				
Northeast	40	19.3	17,191	25.1
Midwest	51	24.6	21,866	31.9
South	63	30.4	17,255	25.2
West	53	25.6	12,266	17.9

[1]Restricted to white subjects who responded to the baseline questionnaire and were cancer-free (other than nonmelanoma skin cancer) at that time. Some frequencies do not total 100% due to missing information.–[2]Based on responses to 1st questionnaire (1984-1989).–[3]Subjects were placed in the "highest" educational category applicable, with college ranked after radiologic training, which was ranked after high school education.

exposure indicator (Table II) disappeared when we adjusted for adult sunlight exposure (data not shown).

Risk associated with job history, work practices and procedures

Melanoma risk was not associated with the age at which a radiologic technologist first worked, nor the total number of years worked as a technologist (Table III). We did, however, find an increased risk associated with beginning work as a radiologic technologist before 1940 (RR = 8.6; 1.0–72.7) compared to beginning in 1970 or later, although this result was based on only 4 cases. After combining the 2 early periods (<1940 and 1940–49), we found an 80% increase in risk among those who began work before 1950 (based on 15 cases), but risk was not increased with beginning work in any subsequent decade. Working 5 or more years prior to 1950 (compared to not working) was associated with higher risk (RR = 2.4; 0.7–8.7), and risk increased significantly (p [trend] = 0.03) with increasing number of years worked prior to 1950. There was no apparent association with years worked in subsequent calendar periods.

When we evaluated melanoma risk associated with years worked before 1950 among those with potentially low residential sunlight exposure (1st–3rd quintiles of proxy variable for adult exposure) and those with high residential sunlight exposure (4th–5th quintiles), risk was increased in the low sunlight group (5+ years < 1950; RR = 9.9; 1.1–86.2), although the number of cases was small (n = 5). Risk was not elevated in the group with high sunlight exposure (RR = 0.7; 0.1–4.9), although again, numbers were very small (n = 2).

We found a nonsignificant increase (RR = 2.2) in risk for technologists who began working with diagnostic procedures before 1950 (compared to the 1970s or later) and a similar increase in risk among those first working with therapeutic procedures before 1950 (Table III), although there were only 4 cases. A modest 50% excess was observed among those who first began working with nuclear medicine in the 1960s.

There was a small, nonsignificant 40% elevated risk associated with not customarily using a lead apron or protective shield when first beginning to work (Table III), based on 14 cases, and a similar level of risk associated with being x-rayed 10 or more times as part of training, based on 9 cases. The practice of holding a patient who was being x-rayed was not associated with elevated risk (Table III). In addition, risk was not linked to exposure to personal therapeutic x-rays, nor to personal diagnostic x-ray exposures (data not shown).

DISCUSSION

This analysis of white men and women certified as radiologic technologists in the U.S. provides suggestive evidence of an increased risk of melanoma following low-to-moderate, chronic radiation exposure. Risk was substantially increased among technologists who first began working before 1940, although based on only 4 cases, and rose with increasing years worked before 1950. That we found no association with the total number of years worked suggests that radiation exposures during early calendar years may be more predictive of risk than total employment duration. The results are consistent with chronic occupational radiation contributing to melanoma because dose levels were likely substantially higher before 1950 than later.[14–16]

The increased risk among radiologic technologists who did not use protective aprons or shields is consistent with the likely higher level of unprotected exposures, as is the increased risk among technologists who were x-rayed numerous times as part of training. The absence of any trend with age first worked suggests no relationship to early age exposures, within the narrow age range involved here. The slightly inverse and nonsignificant associations with holding patients being x-rayed is counterintuitive and may simply be due to chance. The disparate associations with early calendar years worked among those in low and high sunlight regions were unexpected and may be unreliable given the small numbers of technologists working before 1950 in each strata. Alternatively, they may reflect an inability to detect associations with work-related radiation in the presence of a major causal agent such as sunlight or possibly other unknown factors.

TABLE II – ADJUSTED RELATIVE RISKS (RR) AND 95% CONFIDENCE INTERVALS (CI) OF MELANOMA ASSOCIATED WITH DEMOGRAPHIC AND CONSTITUTIONAL FACTORS, PERSONAL AND FAMILY HISTORY OF SKIN CANCER AND POTENTIAL "RESIDENTIAL" SUNLIGHT EXPOSURE INDEX IN THE WHITE STUDY POPULATION OF THE U.S. RADIOLOGIC TECHNOLOGIST COHORT[1]

Characteristics[2]	No. of cases	RR[3]	95% CI	*p* (trend)
Age (at baseline questionnaire[4])				
<35	81	1.0	—	
35–44	78	1.4	1.0–1.8	
45–54	32	1.4	0.9–2.1	
55+	16	1.3	0.7–2.2	0.07
Gender				
Female	159	1.0	—	
Male	48	1.1	0.8–1.5	
Skin tone[5]				
Medium/dark	53	1.0	—	
Fair	140	2.7	2.0–3.7	
Eye color[5]				
Brown/black	41	1.0	—	
Grey/hazel	40	1.3	0.8–2.0	
Blue/green	112	1.9	1.4–2.8	
Hair color[5]				
Dark brown	71	1.0	—	
Light brown	63	1.2	0.8–1.6	
Blonde	37	1.4	0.9–2.1	
Red	22	2.8	1.7–4.4	
Past skin cancer (basal/squamous)				
No	193	1.0	—	
Yes	14	4.5	2.5–7.9	
Family history of melanoma in 1st-degree relatives[5]				
No	185	1.0	—	
Yes	8	5.0	2.5–10.2	
Estimated mean annual adult residential sunlight exposure[6] (quintiles)				
1 (lowest)	40	1.0	—	
2	28	0.9	0.5–1.4	
3	30	0.8	0.5–1.3	
4	42	1.2	0.7–1.8	
5 (highest)	59	1.8	1.2–2.6	<0.001[7]
Estimated mean childhood residential sunlight exposure (quintiles)[8]				
1 (lowest)	50	1.0	—	
2	45	0.9	0.6–1.4	
3	20	0.8	0.5–1.4	
4	34	0.8	0.5–1.3	
5 (highest)	50	1.4	0.9–2.1	0.04[7]

[1]Restricted to white subjects who responded to the baseline questionnaire and were cancer-free (other than nonmelanoma skin cancer) at that time.–[2]Missing information was coded in a separate category (not shown).–[3]Relative risk estimated using Cox proportional hazards regression with age as the time-scale, stratified at baseline by birth cohort in 5-year intervals.–[4]This variable alone was analyzed using follow-up years as the time-scale, with no strata at baseline, in Cox proportional hazards regression. *p* (trend) based on the underlying continuous variable.–[5]Subjects who died of melanoma, and thus did not respond to the second questionnaire, have missing information for these variables.–[6]Time-weighted average of estimated annual solar ultraviolet (in Robertson-Berger units $\times 10^{-4}$) assigned to each state (Scotto, 1996) in which a job was performed and weighted by the duration of the job (quintile cutpoints: 108, 114, 126, 152).–[7]p (Trend) based on the underlying continuous variable.–[8]Estimated annual solar ultraviolet (in Robertson-Berger units $\times 10^{-4}$) assigned to the state of birth (Scotto, 1996) (quintile cutpoints: 105, 113, 117, 142).

There is limited epidemiologic literature on the relationship between ionizing radiation and melanoma, particularly with medical occupational exposures. Many of the medical radiation worker studies, including reports on radiologic technologists in Japan[22] and China,[23] U.S.[24] and British radiologists[25] and Danish radiotherapy staff[26] either do not distinguish between melanoma and nonmelanoma skin cancer outcomes or exclusively evaluate nonmelanoma skin cancer. In contrast, the recent, large Canadian study of cancer and occupational radiation doses[27] with 191,333 subjects (of whom 109,844 worked in dental or medical jobs) found a significantly elevated SIR for melanoma (1.16; 90% CI = 1.04–1.30; $n = 222$). The authors were, however, equivocal about the finding because dental workers, the only occupational category with significant risks, had the lowest doses, and confounder information, such as sun exposure, was unavailable. Similarly, the American Cancer Society case-control study of occupation and melanoma incidence, which was nested in a cohort of 1.2 million volunteer respondents, found a significant risk for melanoma associated with occupational exposure to x-rays, but noted that the contribution of dentists to the finding may have been due to uncontrolled confounders.[28]

Among the large British nuclear worker studies that specifically evaluated melanoma risks, excess melanoma has not been observed.[29,30] These studies, however, analyze mortality rates, which may limit their opportunity to detect risk for diseases with relatively low case fatality rates, such as melanoma.[2] Several studies[31–33] of workers at the Lawrence Livermore National Laboratory (LLNL), where high-energy physics is conducted, found an excess risk of melanoma incidence, including a study that evaluated risks associated with individual radiation dosimetry readings.[9,33] There are questions, however, about the elevated risk because of small case numbers and the absence of excesses at other radiogenic tumor sites. Moreover, similar excesses were not found at LLNL's sister laboratory, Los Alamos National Laboratory.[34]

Several small cohort studies of pilots and flight attendants who are exposed to cosmic radiation during airplane flights have also observed an elevated SIR for melanoma,[35–37] but these included few cases and no information on recreational solar exposures, which may be linked to high socioeconomic status, particularly among pilots. In the recent Japanese atomic bomb survivor study of incident skin cancer,[38] a large, though nonsignificant, excess relative risk point-estimate ($ERR_{1Sv} = 2.1$) for melanoma was

TABLE III – ADJUSTED RELATIVE RISKS (RR) AND 95% CONFIDENCE INTERVALS (CI) OF MELANOMA ASSOCIATED WITH YEARS WORKED AS A RADIOLOGIC TECHNOLOGIST, RADIOLOGIC PROCEDURES USED AND OTHER WORK PRACTICES IN THE WHITE STUDY POPULATION OF THE U.S. RADIOLOGIC TECHNOLOGIC STUDY COHORT[1]

Characteristics	No. of cases	Unadjusted RR[2]	95% CI	*p* (trend)	Multivariate RR	95% CI	*p* (trend)
Age first worked as radiologic technologist							
≤18	63	1.0	—		1.0	—	
19–24	115	0.9	0.6–1.2		0.8	0.6–1.1	
25+	23	0.9	0.5–1.4	0.28	0.7	0.4–1.2	0.12
Total years worked (years)							
<5	37	1.0	—		1.0	—	
5–14	117	0.7	0.5–1.0		0.7	0.5–1.0	
15–24	29	0.5	0.3–0.8		0.5	0.3–0.7	
25+	18	0.9	0.5–1.8	0.23	0.8	0.4–1.6	0.16
Year first worked as a radiation technologist[3]							
1970+	94	1.0	—		1.0	—	
1960-69	62	0.7	0.4–4.1		0.9	0.5–1.4	
1950-59	30	0.9	0.4–2.0		1.1	0.5–2.5	
<1950	15	1.6	0.5–4.7		1.8	0.6–5.5	
1940-49	*11*	*1.4*	*0.4–4.3*		*1.6*	*0.5–5.1*	
<1940	*4*	*7.4*	*1.0–54.9*	0.36	*8.6*	*1.0–72.7*	0.11
No. of years worked <1950[4]							
0	186	1.0	—		1.0	—	
1–4	8	1.4	0.5–4.0		1.5	0.5–4.1	
5+	7	2.6	0.7–9.5	0.03	2.4	0.7–8.7	0.03
No. of years worked in 1950s[4]							
0	161	1.0	—		1.0	—	
1–4	26	1.3	0.7–2.4		1.3	0.7–2.5	
5+	16	0.9	0.4–2.0	0.92	0.9	0.4–1.9	0.85
No. of years worked ≥1960[4]							
0	13	1.0	—		1.0	—	
1–4	34	1.1	0.5–2.4		1.1	0.5–2.3	
5+	156	0.8	0.4–1.6	0.22	0.7	0.4–1.5	0.14
Year first worked with diagnostic procedures.[5]							
1970+	87	1.0	—		1.0	—	
1960-69	60	0.6	0.3–1.1		0.7	0.4–1.2	
1950-59	30	1.2	0.4–3.2		1.4	0.5–3.7	0.11
<1950	13	2.0	0.5–8.2	0.31	2.2	0.5–9.3	
Year first worked with therapeutic procedures.[6]							
1970+	33	1.0	—		1.0	—	
1960-69	19	0.6	0.3–1.1		0.6	0.3–1.1	
<1960	13	1.2	0.5–2.7		1.1	0.5–2.6	
1950-59	*9*	*0.9*	*0.4–2.4*		*0.9*	*0.3–2.4*	
<1950	*4*	*2.2*	*0.6–8.1*	0.73	*2.1*	*0.6–8.0*	0.68
Year first worked with nuclear medicine[7]							
1970+	46	1.0	—		1.0	—	
1960-69	35	1.5	0.8–2.6		1.5	0.9–2.7	
<1960	15	1.0	0.4–2.1		1.0	0.4–2.2	
1950-59	*13*	*1.1*	*0.4–2.6*		*1.1*	*0.4–2.6*	
<1950	*2*	*0.7*	*0.1–3.4*	0.11	*0.8*	*0.2–3.8*	0.13
Used lead apron or shield[8]							
Yes	187	1.0	—		1.0	—	
No	14	1.6	0.9–2.8		1.4	0.8–2.5	
No. times held patient x-rayed[9]							
0	11	1.0	—		1.0	—	
1–9	25	1.0	0.5–2.0		1.0	0.5–2.1	
10–24	32	0.8	0.4–1.6		0.9	0.4–1.7	
25–49	37	0.8	0.4–1.6		0.8	0.4–1.7	
50+	98	0.7	0.4–1.3	0.06	0.7	0.4–1.3	0.08
No. times x-ray practiced on self[9]							
0	184	1.0	—		1.0	—	
1–9	14	0.9	0.5–1.6		0.9	0.5–1.6	
10+	9	1.5	0.8–3.1	0.33	1.4	0.7–2.8	0.53

[1]Restricted to white subjects who responded to the baseline questionnaire and were cancer-free (other than nonmelanoma skin cancer) at that time. RRs based on Cox proportional hazards regression with age as the time-scale, stratified at baseline for birth cohort in 5-year intervals and adjusted for sex, skin tone, hair color, prior nonmelanoma skin cancer, and proxy sunlight radiation exposures. Missing information were coded as separate categories (not shown). Trends based on continuous variables unless otherwise indicated.–[2]Unadjusted RR refers to analysis that did not include the factors listed in footnote 1, year first worked or cumulative number of years worked. However, it does include simultaneous adjustment for years worked in different decades or with different procedures.–[3]Additionally adjusted for total years worked.–[4]Additionally adjusted for years worked in other time periods.–[5]Diagnostic procedures included fluoroscopy, dental, routine x-ray, multifilm and CAT scan. Additionally adjusted for total years worked with diagnostic procedures and year first worked with therapeutic and nuclear procedures and total years worked with therapeutic and nuclear procedures.–[6] Therapeutic procedures included orthovoltage, cobalt 60, betatron and other x-ray teletherapy. Additionally adjusted for total years worked with therapeutic procedures and year first worked with diagnostic and nuclear procedures and total years worked with diagnostic and nuclear procedures.–[7]Nuclear procedures included diagnostic radioisotopes, radium therapy and other radioisotope therapy. Additionally adjusted for total years worked with nuclear procedures and year first worked with diagnostic and therapeutic procedures and total years worked with diagnostic and therapeutic procedures.–[8]Usual practice when first began working. Additionally adjusted for year first worked.–[9]Additionally adjusted for year first worked. Trend based on ordered categories.

observed but was based on only 10 cases. Thus, while several studies provide suggestive evidence of a potential association between radiation exposure and melanoma, small numbers of cases, lack of incidence data and inability to control for potential confounders prevent solid inferences about the nature of the relationship.

The USRT study is one of the few large prospective cohort studies of low-to-moderate, chronic radiation exposure to radiation workers and melanoma. Its strengths compared to previous studies include the relatively large number of cases overall, the collection of incident cases as well as cancer deaths and the availability of information on some major potential confounders, including constitutional and personal and family medical history.

The major limitation to understanding the elevated risk of melanoma associated with early employment as a medical radiation worker is the lack of individual dosimetry data, particularly for the early work years. Another important limitation is the inability to validate all the self-reported melanomas and death certificate melanoma cases. The high validation rate for self-reported melanomas, however, supported using unvalidated cases, and the results of analyses limited to validated cases was generally similar to the findings reported here except where there were small numbers of validated cases.

A further limitation was that decedent cases, unlike incident cases, did not have covariate information on constitutional factors or date of diagnosis. However, this is not likely a substantial problem because deaths due to melanoma constituted only 7% of all cases, covariates had limited effect on the findings (as indicated in Table III), follow-up time for incident and decedent cases was similar and most importantly, findings based on incident cases alone were similar to the results for incident cases plus melanoma cases identified from death certificates. Other limitations include the small number of cases contributing to the excesses observed, particularly in the exploratory analysis of interaction between sunlight exposure and occupational ionizing radiation. A further limitation was the lack of individual worker information on sunlight exposure (especially from birth to year of first employment), sunburn history and number of nevi. As to sun exposure, however, the relatively uniform occupational history of the subjects offers an advantage over less homogeneous worker populations and those using an external referent because the internal comparison population in this cohort likely shares patterns of sunlight exposure during the work week.

Despite the limitations, the credibility of the associations in our present study was enhanced by our finding the expected relationships between melanoma and established risk factors for which data was available, including fair skin, blue or green eyes, red hair, previous nonmelanoma skin cancer and a family history of melanoma. Moreover, the magnitude of risks related to constitutional and skin cancer history variables was generally consistent with previous findings.[7,20,39,40] The level of risk associated with proxy measures of adult residential sunlight was also consistent with the epidemiologic literature.[41]

In summary, although based on small numbers, the risk of melanoma in the USRT cohort increased significantly with increasing number of years worked before 1950, when ionizing radiation exposures were likely highest. There was also a suggestion of increased risk from performing radiation procedures without a lead apron or protective shield and from being x-rayed as part of radiologic training. Clarifying the possible role of exposure to chronic ionizing radiation in melanoma is likely to require nested case-control studies within occupational cohorts, such as this one, which will assess individual radiation doses, and detailed information about sun exposure, sunburn history and skin susceptibility characteristics.

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